Research Article

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Risk Factors for Venous Thromboembolism in Hospitalized Patients in the Chinese Population

Abstract: Venous thromboembolism (VTE) refers to the formation of a blood clot inside veins and has a high risk of inducing medical accidents. An effective risk assessment model will help screen high risk populations and prevent the occurrence of VTE. In this study, 287 VTE cases were collected and analyzed for risk factors in a Chinese population. The risks of VTE were evaluated using the Caprini and Padua models. Our results indicated that the Caprini model was more effective in evaluating VTE risk among hospitalized patients than the Padua model. As well, the Caprini model was more relevant in VTE risk assessment among surgery patients compared with internal medicine patients, while the Padua model showed no significant differences. In our studies, the most frequent risk factors included obesity, medical patients currently at bed rest, and severe lung disease. Our studies provide clinical support on selecting the suitable risk assessment model of VTE in the Chinese population.

Keywords: Caprini model; Padua model; risk assessment; risk factors; venous thromboembolism

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1 Introduction

Venous thromboembolism (VTE) refers to the formation of a blood clot (thrombus) inside veins. The clinically predominant sites of VTE are in the vessels of the leg and the lungs, which result in deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), respectively. VTE appears in different hospital departments, and has a high risk of inducing medical accidents and tangles [1-3]. However, it is possible to reduce the occurrence of VTE if effective prevention measures are adopted [4]. At present, guidelines have been introduced by different countries and organizations to emphasize the importance of VTE prevention. The World Health Organization (WHO, 2009) has included the prevention of VTE into the surgical safety evaluation criteria [5].

The prerequisite of VTE prevention is to find an effective risk assessment model, which helps screen for populations at high risk of VTE. Different risk assessment models of VTE have been proposed, each having its own application fields and limitations [6-11]. The Caprini risk assessment model was established by JA Caprini in 2005, and is primarily used for surgical non-orthopedic patients [7]. The guidelines issued by the American College of Chest Physicians (ACCP) recommended using the Caprini model to evaluate the VTE risks among surgical inpatients, including general surgery, vascular surgery and urinary surgery, plastic surgery, orthopedics, etc [12, 13]. The validity of this model has been verified by clinical practice in different countries [14-17].

At present, there is limited evidence on VTE risk assessment for medical inpatients. Barber and colleagues reported that the Padua model was effective in screening patients with high risk of VTE among medical inpatients [10]. Clinical research indicated that the scores based on the Padua model were highly correlated to the incidence of VTE-related deaths in medical patients [18]. The guidelines issued by ACCP recommended using the Padua model to evaluate the VTE risks among medical inpatients [19].

It remains to be verified whether the existing VTE risk assessment models universally apply to different races and

different regional populations. Abundant clinical data are required to help select the appropriate model for specific populations. In this study, 287 VTE cases were collected and analyzed for risk factors in a Chinese population. The risks of VTE were evaluated using the Caprini and Padua models.

2 Materials and Methods

2.1 Patients

387 VTE cases, including both DVT and PTE symptoms, were collected in China Meitan General Hospital and Chaoyang Hospital for a duration of 12 months (Jan 2012 to Dec 2012). DVT was determined by venous color Doppler ultrasonography or venography, while PTE was diagnosed by spiral computed tomography angiography (CTA), pulmonary arteriography (PAG), perfusion scanning or radionuclide pulmonary ventilation. Among the 387 VTE cases, 287 patients who satisfied the following criteria were included in the study: (1) hospitalizations not related to VTE treatment; (2) hospital stay exceeding 2 days; and (3) over 18 years old. Two investigation methods were applied to the selected VTE patients, including a retrospective and follow-up study.

Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has approved by the Institutional Review Board of China Meitan General Hospital and its affiliated Chaoyang Hospital.

2.2 Retrospective Study

Clinical and demographic information, as well as laboratory and imageology examination results were collected for the 287 VTE cases (including name, gender, age, height, weight, hospitalization date, hospitalization department, hospital stay duration, VTE risk factors). Risk factors of VTE were analyzed by the Padua (Table 1) or Caprini model (Table 2). For the Padua model, patients with a cumulative score less than 4 had a low risk of developing VTE; otherwise, they were regarded as high-risk patients. For the Caprini model, the risk levels were defined as follows: (1) Low risk (cumulative risk score 0-1); (2) Moderate risk (cumulative risk score 2); and (3) High risk (cumulative risk score ≥3).

2.3 Follow-up Study

Informed consent forms were signed by all the subjects or their legal guardians. The follow-up lasted between 24 and 36 months (30 months in average). The follow-up items included: (1) re-examination results of VTE after being discharged, e.g. venous color Doppler ultrasonography, venography, spiral CTA, PAG, perfusion scanning and radionuclide pulmonary ventilation; (2) evaluation of whether or not the patient continued to take anti-clotting drugs after leaving the hospitals and the duration thereof;

Table 1. Risk Assessment of VTE by the Padua Model

Risk factors	Score
Previous VTE (with the exclusion of superficial vein thrombosis)	
Active cancer	
Reduced mobility	3
Already known thrombophilic condition	
Recent (<1 month) trauma and/or surgery	2
Elderly age (≥70 years)	
Heart and/or respiratory failure	
Acute myocardial infarction or ischemic stroke	
Obesity (BMI≥30)	1
Acute infection and/or rheumatologic disorder	
Ongoing hormonal treatment	

Table 2. Risk Assessment of VTE by the Caprini Model

Risk factors	Score
Stroke	
Multiple trauma	
Elective major lower extremity arthroplasty	5
Hip, pelvic or leg fracture	
Acute spinal cord injury (paralysis)	
Age (≥75)	
History of DVT or PTE	
Positive Factor V Leiden	
Positive prothrombin G20210A	
Elevated serum homocysteine	
Positive lupus anticoagulant	3
Other congenital or acquired thrombophilia	
Geparin-induced thrombocytopenia (HIT)	
Family history of VTE	
Elevated anticardiolipin antibodies	
Age (61-74)	
Central venous access	
Arthroscopic surgery	
Major surgery	
Malignancy	2
Laparoscopic procedure >45 min	
Patient confined to bed	
Immobilizing plaster cast	
Age (41-60)	
Acute myocardial infarction	
Heart failure	
Varicose veins	
Obesity (BMI>25)	
Inflammatory bowel disease	
Sepsis	
COPD or abnormal pulmonary function	
Severe lung disease	1
Oral contraceptives or HRT	
Pregnancy or postpartum	
History of unexpected stillborn infant, recurrent spontaneous abortion (≥3), premature birth with toxemia or growth-restricted infant	
Medical patient currently at bed rest	
Minor surgery planned	
History of prior major surgery	
Swollen legs	

and (3) outcome of diseases, e.g. disease resolution or recurrence. Of the 287 VTE cases, 260 patients were followed up successfully, because 11 patients died from non-VTE factors and another 16 patients were not able to be contacted during the first follow-up. For the 11 dead patients, 5 of them died from cancer or serious pulmonary infection within the first year of follow-up, and 6 of them died from cancer, heart failure or stroke during the second year of follow-up.

2.4 Statistical Analysis

Continuous variables with a normal distribution were presented as means with standard deviations. Continuous variables with a skewed distribution were presented as median values with interquartile ranges. Discrete variables were presented as frequencies and percentages. The chi square test was used to compare the differences between

Caprini and Padua models in assessing the risks of VTE in hospitalized patients. Independent sample T test was used to compare the differences of VTE risk assessment among surgical and medical patients. Bilateral p < 0.05 was considered to be statistically significant.

3 Results

In total, 287 valid VTE cases were collected, including DVT and PTE symptoms. The clinical information of these VTE cases is shown in Table 3. Of the 287 VTE cases, 92 patients (32.1%) showed DVT symptoms, 93 patients (32.4%) showed PTE symptoms and 103 (35.9%) patients showed both DVT and PTE symptoms. The male to female ratio was about 1:1. The ages of the patients ranged from 20 to 99, with a median age of 66 and 114 of the patients (39.6%) were over 70 years old. Of the 287 VTE cases, 155 patients (54.0%) were from internal medicine departments, including respiratory, intensive care unit, cardiology, geriatrics, neurology, tumor, nephrology, infection, hematology, endocrinology, gastroenterology, and occupational disease; 133 patients (46.0%) were from surgery departments, including vascular surgery, obstetrics and gynecology, neurosurgery, general surgery, urinary surgery, thoracic surgery, ear, nose and throat, and orthopedics. We collected 190 valid data units of body mass index (BMI), ranging from 16 to 40 kg/m^2, with a median value of 25 kg/m^2. About 63% of patients had a BMI value over 25 kg/m^2.

The distribution of VTE risk factors based on the Caprini model is shown in Table 4. The most frequent risk factors included BMI > 25 kg/m^2 (120/190, 63.2%), medical patients currently at bed rest (136/287, 47.4%), and severe lung disease (132/287, 46.0%). The standard of elevated serum homocysteine levels was defined as 15 μmol/L, and 9 patients (50%) had elevated serum homocysteine levels out of 18 patients with valid data. For anticardiolipin antibody examination, 9 patients (13.4%) were positive among 67 cases with valid data. For protein C or protein S examination, 32 patients (52.4%) had protein C or protein S deficiency among 61 cases with valid data. Studies of Factor V Leiden, prothrombin G20210A and lupus anticoagulant were not performed.

For the Caprini model, most patients (95.5%) were classified as high risk (Figure 1A). For the Padua model, 109 patients (38.0%) were classified as low risk, while 178 patients (62.0%) were classified as high risk (Figure 1B). The percentage of high risk patients based on the Caprini model was significantly higher than that based on the Padua model (Table 5, p < 0.0001), which indicated that

Table 3. Clinical Information of VTE Patients

Clinical Index		Case Number	Percentage
Symptom	DVT	92	32.1%
	PTE	93	32.4%
	DVT and PTE	103	35.9%
	Total	287	100.0%
Gender	Male	141	49.1%
	Female	146	50.9%
	Total	287	100.0%
Age	20~29	9	3.1%
	30~39	14	4.9%
	40~49	25	8.7%
	50~59	49	17.1%
	60~69	76	26.5%
	≥70	114	39.7%
	Total	287	100.0%
Department	Internal medicine	155	54.0%
	Respiratory	47	16.4%
	Intensive care unit	15	5.2%
	Cardiology	15	5.2%
	Geriatrics	14	4.9%
	Neurology	11	3.8%
	Tumor	9	3.1%
	Nephrology	8	2.8%
	Infection	8	2.8%
	Hematology	8	2.8%
	Endocrinology	8	2.8%
	Gastroenterology	6	2.1%
	Occupational disease	6	2.1%
	Surgery	131	45.6%
	Vascular surgery	42	14.6%
	Obstetrics and Gynecology	25	8.7%
	Neurosurgery	12	4.2%
	General surgery	11	3.8%
	Urinary surgery	11	3.8%
	Thoracic surgery	11	3.8%
	Ear, nose and throat	11	3.8%
	Orthopedics	9	3.1%
	Total	287	100.0%
BMI	< 25 kg/m^2	70	36.8%
	25~28 kg/m^2	73	38.4%
	> 28 kg/m^2	47	24.7%
	Total	190	100.0%

A Caprini model
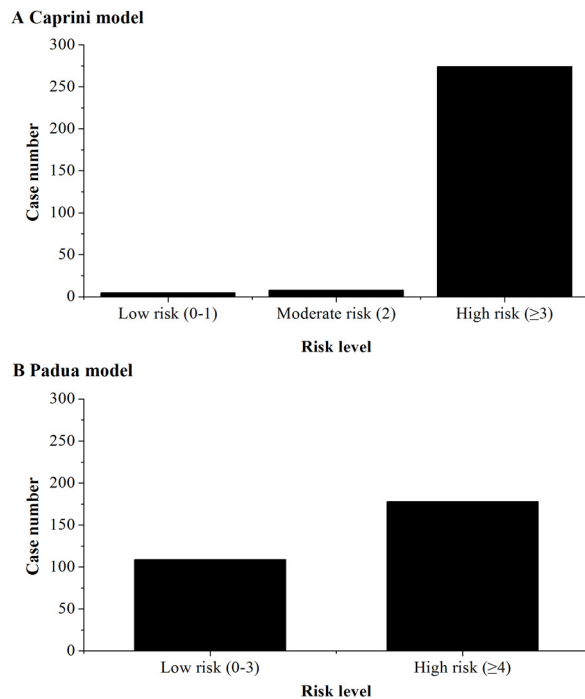

B Padua model

Figure 1 Risk levels of VTE Patients by the Caprini (A) and Padua (B) model

the Caprini model was more effective in evaluating the VTE risks among hospitalized patients. Of the 287 VTE cases, 155 patients (54.0%) were from internal medicine departments, and 133 patients (46.0%) were from non-orthopedic surgery departments. In the Padua model, the average cumulative risk scores for internal medicine and surgery showed no significant differences (4.43 ± 2.65 vs. 4.42 ± 2.83, $p = 0.962$, Table 6). By contrast, in the Caprini model, the average cumulative risk score for surgery patients was significantly higher than internal medicine patients (7.84 ± 3.45 vs. 6.68 ± 3.27, $p = 0.004$, Table 7). These results indicate that the Caprini model was more effective in evaluating the VTE risks among surgery patients compared with internal medicine patients.

Among the 260 follow-up patients, 15 patients did not take any anticoagulant drugs after they were initially diagnosed as VTE; as well, 48 patients were diagnosed as recurrent VTE. The recurrence rate for high risk patients was 19.4% (48/247), while there was no recurrence among low or moderate risk patients (Figure 2). Of the 48 patients, 3 patients did not take any anticoagulant drugs after being initially diagnosed as VTE, while recurrent VTE occurred in 45 patients after they stopped the anticoagulant treatment.

Table 4. VTE Risk Factors of Patients in the Caprini Model

Factor	Score	Case Number	Percentage
Age (41~60)	1	84	29.3%
Acute myocardial infarction	1	4	1.4%
Congestive heart failure	1	68	23.7%
Varicose veins	1	37	12.9%
Obesity (BMI>25)&	**1**	**120**	**63.2%**
Inflammatory bowel disease	1	3	1.0%
Sepsis (< 1 month)	1	6	2.1%
COPD or abnormal pulmonary function	1	106	36.9%
Severe lung disease, including pneumonia (< 1 month)	**1**	**132**	**46.0%**
Oral contraceptives or HRT	1	2	0.7%
Pregnancy or postpartum (< 1 month)	1	2	0.7%
History of unexpected stillborn infant, recurrent spontaneous abortion (≥3), premature birth with toxemia or growth-restricted infant	1	16	5.6%
Medical patient currently at bed rest	**1**	**136**	**47.4%**
Minor surgery planned	1	10	3.5%
History of prior major surgery (< 1 month)	1	39	13.6%
Swollen legs	1	117	40.8%
Age (61-74)	2	101	35.2%
Central venous access	2	7	2.4%
Arthroscopic surgery	2	0	0.0%
Major surgery (> 45 min)	2	20	7.0%
Malignancy (past or present)	2	80	27.9%
Laparoscopic procedure (> 45 min)	2	7	2.4%
Patient confined to bed (> 72 h)	2	39	13.6%
Immobilizing plaster cast (< 1 month)	2	1	0.3%
Age ≥ 75	3	78	27.2%
History of DVT or PTE	3	34	11.8%
Positive Factor V Leiden; positive prothrombin G20210A; positive lupus anticoagulant§	3	-	-
Elevated serum homocysteine	3	9	50.0%
Elevated anticardiolipin antibodies	3	9	13.4%
Other congenital or acquired thrombophilia (protein C or protein S deficiency)*	3	32	52.4%
Heparin-induced thrombocytopenia (HIT)	3	0	0.0%
Family history of VTE	3	11	3.8%
Stroke (< 1 month)	5	19	6.6%
Acute spinal cord injury (paralysis) (< 1 month)	5	5	1.7%
Multiple trauma (< 1 month)	5	2	0.7%
Hip, pelvic or leg fracture (< 1 month)	5	10	3.5%
Elective major lower extremity arthroplasty	5	1	0.3%

&190 valid cases; §not performed yet; 18 valid cases; 67 valid cases; *61 valid cases.

Table 5. Number of VTE patients by risk level and cumulative score in two risk assessment models

Risk grade	Caprini model*, cases (%)	Padua model§, cases (%)	p#
Low-moderate	13 (4.5)	109 (38.0)	<0.0001
High	274 (95.5)	178 (62.0)	
Cumulative score, mean ± STD or median (interquartile range)	7.21±3.40	4 (3-6)	

* For Caprini model, the risk levels were defined as follows: (1) Low risk (cumulative risk score 0-1); (2) Moderate risk (cumulative risk score 2); (3) High risk (cumulative risk score ≥3).

§ For Padua model, the risk levels were defined as follows: (1) Low risk (cumulative risk score 0-3); (2) High risk (cumulative risk score ≥4).

chi square test

Table 6. Patients classified to different risk level in department of internal medicine and surgery by Padua Model

Risk grade	Internal medicine, cases (%)	Surgery, cases (%)	p
Low risk (0-3)	56 (36.1)	53 (40.2)	
High risk (≥4)	99 (63.9)	79 (59.8)	
Cumulative score, mean ± STD	4.43±2.65	4.42±2.83	0.962*

* Independent sample T test

Table 7. Patients classified to different risk level in department of internal medicine and surgery by Caprini Model

Risk grade	Internal medicine, cases (%)	Surgery, cases (%)	p
Low risk (0-1)	4 (2.6)	1 (0.8)	
Moderate risk (2)	5 (3.2)	3 (2.3)	
High risk (≥3)	146 (94.2)	128 (96.9)	
Cumulative score, mean ± STD	6.68±3.27	7.84±3.45	0.004*

* Independent sample T test
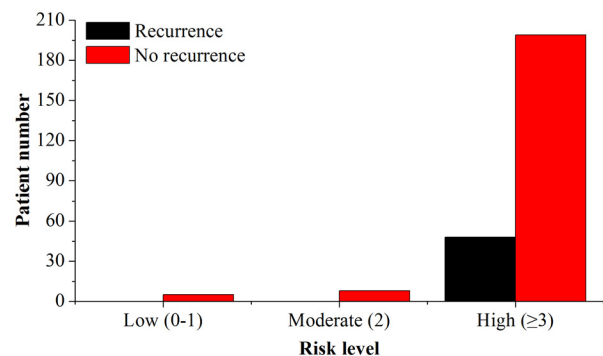
Figure 2 Risk levels and recurrence of 260 follow-up patients by the Caprini model

4 Discussion

In this study, 287 VTE cases were collected within the Chinese population, and evaluated for risk factors using the Caprini and Padua models. Our results showed that the Caprini model was more effective in evaluating VTE risks in hospitalized patients compared with the Padua model, which is consistent with a previous study in the Chinese population [15]. The Caprini model includes over 40 risk factors, which provides more comprehensive and reasonable risk assessment than the Padua model.

Our results suggested that the Caprini model was more relevant in VTE risk assessment among surgery patients compared with internal medicine patients. Indeed, the Caprini model has been applied mainly to surgical patients, which may be due to the fact that this model contains more surgical factors [12, 13]. There has been limited research on the VTE risk assessment for medical inpatients so far. It was reported that the Padua model was effective in screening patients with high risk of VTE among medical inpatients [10]. However, the Padua model showed no significant difference in evaluating VTE risks between internal medicine and surgical patients in our studies.

In our studies, the most frequent risk factors of VTE included obesity, medical patients currently at bed rest, and severe lung disease. The ENDORSE study showed that obesity and long-term bed rest were two of the most common risk factors for VTE in surgical inpatients [20]. It was reported that obesity increased the risk of

recurrent VTE [21]. The sixth and seventh session of ACCP included obesity as the risk factor of DVT in orthopedics perioperative period. The mechanism of VTE formation in obese patients may be related to blood stasis. For patients in a long-term bed ridden state, the potential causes of VTE include slow flow velocity, local blood stasis, and high coagulation state.

Our results showed that severe pulmonary disease is another high risk factor of VTE occurrence. The incidence of PTE in patients with chronic obstructive pulmonary disease (COPD) ranged from 20% to 60%. It was regarded that the mechanism of VTE occurrence is mainly attributed to the pre-thrombosis state of COPD. In addition, the high blood coagulation state induced by long-term lying in bed and repeated infection may be one cause of increased VTE risk. The mechanism of VTE in patients with severe pulmonary disease remains to be further investigated.

Prothrombin (also called coagulation factor II) is proteolytically cleaved to form thrombin during the clotting process, which then catalyzes many coagulation-related reactions as a serine protease. Prothrombin G20210A is a genetic mutant associated with increased risk of VTE, and is mostly present in Caucasians [22]. Coagulation factor V is an important cofactor in the coagulation process, which triggers coagulation by activating prothrombin. Factor V Leiden is the most common genetic hypercoagulability (prone to clotting) mutant in Caucasians, but can be rarely found in Asian and African populations [23, 24]. Therefore, we did not perform prothrombin G20210A and Factor V Leiden studies in the Chinese population. Lupus anticoagulant is an autoantibody which increases inappropriate blood clotting. Lupus anticoagulant testing was not performed in our studies due to limitation of experimental conditions. The association of Lupus anticoagulant and VTE in the Chinese population needs to be further investigated.

In conclusion, the Caprini and Padua models were used for risk assessment of VTE in the Chinese population. Our results indicated the Caprini model was more effective in evaluating VTE risks among hospitalized patients, especially for surgery patients. The most frequent risk factors included obesity, medical patients currently at bed rest and severe lung diseases. This study was limited by a relatively low sample size. In the future, more data need to be collected and studied to provide generalizable conclusions and to help determine the most suitable risk assessment model of VTE in the Chinese population

Conflict of interest: Authors state no conflict of interest.

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